

The claims that read on the elected species as defined by the Examiner are: claims 1-13, and 33-44, and 46-62.

In response to the Examiner's request to comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, 37 C.F.R. §§ 1.821-1.825, that accompanied the Office Action mailed April 5, 2001, Applicants submit herewith the required paper copy and computer readable copy of the Sequence Listing. Please amend the specification in adherence with 37 C.F.R. §§ 1.821-1.825 as follows.

In the Specification:

Please replace the paragraph beginning at page 12, line 23, with the following:

91 --Figure 7 illustrates the self-similarity of Fis binding sites. The sequence logo for Fis (SEQ ID NO:4) (Schneider & Stephens (1990) *Nucl. Acids Res.*, 18: 6097-6100; Hengen *et al.* (1997) *Nucl. Acids Res.*, 25(24): 4994-5002) is shown three times. The upper and lower logos are shifted +11 and +7 bases to the right (respectively) relative to the middle logo. The cosine wave, with a wavelength of 10.6 bases, shows that the +11 relatively shifted Fis sites would be on the same face of the DNA, while the +7 relatively shifted Fis sites would be on opposite faces. Arrows are at positions where the logo is self-similar after a shift. Down arrows mean that the contacts by Fis to the bases would interfere because they would be on the same face of the DNA. Up arrows mean that the contacts could be simultaneous because they are on opposite faces.--

Please replace the paragraph beginning at page 13, line 1, with the following:

92 --Figures 8a, 8b, and 8c illustrate the oligonucleotide design of overlapping and separated Fis binding sites. The predicted Fis sites are shown by walkers floating below each DNA sequence (Schneider (1997) *Nucl. Acids Res.*, 25: 4408-4415; Hengen *et al.* (1997) *supra.*). In a walker, the vertical box marks the zero base of the binding site. The box also shows the vertical scale, with the upper edge being at +2 bits and the lower edge being at -3 bits. The height of each letter is determined from the bit value in the Riw(b,l) matrix (Schneider (1997) *J. Theoret. Biol.*, 189(4): 427-441; Schneider (1997) *Nucl. Acids Res.*, 25: 4408-4415; Hengen *et al.* (1997) *supra.*). Negative weights are represented by drawing the letter upside-down and placing it below the zero bit level. Three DNAs were designed, each having two Fis sites spaced 11 (SEQ ID NO:2), 7 (SEQ ID NO:3) and 23 (SEQ ID NO:5) bases apart. Design details are given in Example 1, Materials and Methods. The total strength of a site is the sum of the information weights for each base. The 18.1 bit Fis sites (SEQ ID NOS: 6 and 7) are 3.4 standard deviations higher than the average Fis site in natural sequences (Hengen *et al.* (1997) *supra.*; Schneider

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(1997) *J. Theoret. Biol.*, 189(4):427-441). The 12.7 (SEQ ID NOS:8 and 9) and 15.0 (SEQ ID NOS:10 and 11) bit sites are 1.6 and 2.4 standard deviations above average (respectively).--

Please replace the paragraph beginning at page 13, line 28, with the following:

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--Figure 10 shows the positions of Fis and DnaA sites at the *Escherichia coli* origin of replication (*oriC*). Sequence data are from GenBank accession K01789. The horizontal dashes below the sequence (SEQ ID NO:12) represent regions protected by Fis. Locations of DnaA sites are from Messer *et al.* (1991) *Res. Microbiol.* 142: 119-125). The asymmetric DnaA individual information matrix was created from 27 experimentally demonstrated DnaA binding sites (data not shown). DNA synthesis start sites are indicated by the arrows at the bottom (Seufert & Messer (1987) *EMBO J.* 6: 2469-2472). The boxes mark two Fis sites separated by 11 bases (SEQ ID NOS:13 and 14). Fis sites with positive individual information are marked from -7 to +7 but evaluated from -10 to +10 according to the matrix. DnaA site directionality is indicated by letters turned sideways in the direction that DnaA binds (Schneider (1997) *Nucl. Acids Res.*, 25: 4408-4415).--

Please replace the paragraph beginning at page 54, line 11, with the following:

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--Synthetic DNAs containing strong Fis sites separated by 11 and 7 base pairs were designed by selecting from the most frequent bases at each position in the Fis sequence logo (Hengen *et al.* (1997) *supra.*). These were then merged with the same sequence shifted by 11 or 7 base pairs by comparing the $R_{iw}(b,l)$ values for various choices. (Note: the consensus sequence of the early model we used was TTTG(G/C)TCA AAATTTGA(G/C)C AAA (SEQ ID NO:1) which differs from that of the logo.) Five extra bases were added to the ends based on the natural sequences around the *hin* proximal and medial sites for the overlap 11 oligo, and the sequences around *cin* external and proximal sites were used for the overlap 7 oligo (Hengen *et al.* (1997) *supra.*). The DNAs were made self complementary (Fig. 8a, 8b). Sites separated by 23 bases were created starting with the 11 base separated DNA and duplicating the central overlap region. A *Bam*HI site was also inserted and the DNA was flanked by *Eco*RI sites (Fig. 10c). Oligonucleotides were synthesized with biotin on the 5' end and gel purified (Oligos Etc., Wilsonville, OR, USA). To ensure thorough annealing, they were heated to 90°C for 10 minutes, and slowly cooled to room temperature. The annealed products were electrophoresed through an 8% (w/v) polyacrylamide gel, and the bands corresponding to the linear duplex DNA of the correct size were sliced from the gel. DNA was recovered by electroelution and extracted with isoamyl alcohol to remove ethidium bromide. A non-specific control DNA was composed of the